PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 95.81434/04	**FOR FURTHER ACTION**	See Form PCT/IPEA/416
International application No. PCT/GB2004/003387	International filing date *(day/month/year)* 04.08.2004	Priority date *(day/month/year)* 04.08.2003
International Patent Classification (IPC) or national classification and IPC B01J13/00, B01J13/02		
Applicant CAMURUS AB		

1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 4 sheets, including this cover sheet.
3. This report is also accompanied by ANNEXES, comprising:
   a. ☒ *sent to the applicant and to the International Bureau)* a total of four sheets, as follows:
      ☐ sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).
      ☐ sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.
   b. ☐ *(sent to the International Bureau only)* a total of (indicate type and number of electronic carrier(s)) , containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).

4. This report contains indications relating to the following items:

☒	Box No. I	Basis of the opinion
☐	Box No. II	Priority
☐	Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
☐	Box No. IV	Lack of unity of invention
☒	Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
☐	Box No. VI	Certain documents cited
☐	Box No. VII	Certain defects in the international application
☐	Box No. VIII	Certain observations on the international application

Date of submission of the demand	Date of completion of this report
06.06.2005	03.11.2005
Name and mailing address of the International preliminary examining authority: European Patent Office - P.B. 5818 Patentlaan 2 NL-2280 HV Rijswijk - Pays Bas Tel. +31 70 340 - 2040 Tx: 31 651 epo nl Fax: +31 70 340 - 3016	Authorized Officer Willsher, C Telephone No. +31 70 340-2649

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/GB2004/003387

Box No. I Basis of the report

1. With regard to the **language**, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.

   ☐ This report is based on translations from the original language into the following language , which is the language of a translation furnished for the purposes of:
   - ☐ international search (under Rules 12.3 and 23.1(b))
   - ☐ publication of the international application (under Rule 12.4)
   - ☐ international preliminary examination (under Rules 55.2 and/or 55.3)

2. With regard to the **elements*** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:

Description, Pages	
1-64	as originally filed
Claims, Numbers	
1-32	received on 04.07.2005 with letter of 30.06.2005
Drawings, Sheets	
1/13-13/13	as originally filed

   ☐ a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing

3. ☐ The amendments have resulted in the cancellation of:
   - ☐ the description, pages
   - ☐ the claims, Nos.
   - ☐ the drawings, sheets/figs
   - ☐ the sequence listing *(specify)*:
   - ☐ any table(s) related to sequence listing *(specify)*:

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).
   - ☐ the description, pages
   - ☐ the claims, Nos.
   - ☐ the drawings, sheets/figs
   - ☐ the sequence listing *(specify)*:
   - ☐ any table(s) related to sequence listing *(specify)*:

* *If item 4 applies, some or all of these sheets may be marked "superseded."*

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/GB2004/003387

Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-32
	No:	Claims	
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-32
Industrial applicability (IA)	Yes:	Claims	1-32
	No:	Claims	

2. Citations and explanations (Rule 70.7):

see separate sheet

1. Following receipt of claims 1-32 with the letter dated 30.06.05, full examination is possible. The observations made in the said letter are noted; nevertheless, the IPEA considers US-A-5 531 925 (Document D1) to be very relevant.

2. D1 describes a method in which a local, dispersible phase is created in the presence of a solvent within a homogenous non-lamellar phase, followed by fragmentation to form particles having an interior made of the homogeneous phase and a surface made of the dispersible phase; the local dispersible phase can be selected as lamellar (claim 7). D1 thus involves a dispersion of lamellar and optionally non-lamellar particles (which are also amphiphilic - see column 1, lines 10-11). Fragmentation can involve co-equilibriation with an amphililic substance at elevated temperature followed by rapid cooling, and can control particle size distribution (column 10, lines 30-31; column 10, line 66 to column 11, line 9; column 11, lines 24-26), and the solvent is most often water or any other polar solvent (column 8, lines 54-56; claims 13 and 33). Since in claim 7 of D1 a lamellar phase must be selected as the local dispersible phase, the method recited in present claim 1 is formally novel. However, its selection from claim 7 of D1 does not involve an inventive step, since D1 clearly indicates that particle size distribution can be controlled, which is also the technical problem posed in the present application (description, page 1, first paragraph).

3. Claims which depend on present claim 1 involve either results to be achieved - ie. no further technical details of the method are given - see claims 2-4 - or subject-matter which has not been shown as inventively contributing to solving the technical problem. The subject-matter of claims 2-14 thus does not involve and inventive step.

4. From the argumentation set forth in paragraph 2, above, the IPEA can see no inventive merit in the particles recited in present claims 15 and 16, and from the argumentation in paragraph 3, above, no inventive step for the subject-matter of present claims 17-32. In this respect, attention is drawn to the abstract of D1, as well as to column 27, lines 42-55).

5. Claims 1-32 are not allowable under Article 33(3) PCT.

Claims

1. A method for the production of amphiphile particles having incorporated therein at least one active agent, said method comprising forming a dispersion of particles comprising at least one amphiphilic structuring agent, followed heating said dispersion to an elevated temperature in a solution of at least one active agent, and then cooling to around ambient temperature.

2. A method as claimed in claim 1 wherein said heating is to a temperature and for a period sufficient to provide, after cooling, an incorporation of active agent into said particles which is at least 130% of the maximum incorporation provided by equilibrating said particles in a solution of at least one active agent at 37°C for up to 3 days.

3. A method as claimed in claim 1 or claim 2 wherein said particles are colloidal.

4. A method as claimed in any of claims 1 to 3 wherein said heating is to a temperature in the range 75°C to 200°C.

5. A method as claimed in any of claims 1 to 4 wherein said heating is for a period of between 1 minute and 4 hours.

6. A method as claimed in any of claims 1 to 5 wherein, prior to incorporation of said active agent, at least 75% by volume of said particles are of non-lamellar or micellar phase.

7. A method as claimed in any of claims 1 to 6 wherein, after incorporation of said active agent, at least 75% by volume of said particles are of non-lamellar or micellar phase.

8. A method as claimed in any of claims 1 to 7 wherein, before incorporation of said active agent, the equilibrium form of the particles is non-lamellar or micellar.

9. A method as claimed in any of claims 1 to 8 additionally comprising drying the amphiphile particles having incorporated therein at least one active agent.

10. Amphiphile particles comprising at least one structure forming amphiphile and an active agent, wherein the incorporation of said active agent into said particles is at least 130% of the maximum incorporation provided by incubating equivalent particles not comprising any active agent in a solution of an excess of said active agent at 37°C.

11. Amphiphile particles as claimed in claim 10, having incorporated therein at least one active agent, said particles being formed by the method of any of claims 1 to 10.

12. Amphiphile particles as claimed in claim 10 or claim 11 wherein said structure forming amphiphile is one or more amphiphiles selected from natural lipids, synthetic lipids, surfactants, and amphiphilic copolymers.

13. Amphiphile particles as claimed in any of claims 10 to 12 wherein a portion of said structure forming amphiphile is a fatty acid and/or an oily amphiphile.

14. Amphiphile particles as claimed in any of claims 10 to 13 wherein said particles are colloidal.

15. Amphiphile particles as claimed in any of claims 10 to 14 wherein the particles are at least 75% by volume non-lamellar or micellar particles or mixtures thereof.

16. Amphiphile particles as claimed in any of claims 10 to 15 additionally comprising at least one fragmenting agent.

17. Amphiphile particles as claimed in claim 16 wherein said fragmenting agent is a surfactant with a hydrophilic lipophilic balance of at least 12.

18. Amphiphile particles as claimed in any of claims 10 to 17 wherein said particles are stable to the loss of said active agent for at least 24 hours at 25°C.

19. Amphiphile particles as claimed in any of claims 10 to 18 wherein said particles are stable in terms of particle size for at least 24 hours at 25°C.

20. A pharmaceutical composition comprising amphiphile particles as claimed in any of claims 10 to 19 and at least one pharmaceutically tollerable carrier or excipient.

21. A powder comprising particles as claimed in any of claims 10 to 20, optionally with some or all of the water therein removed.

22. A gel of cream comprising particles as claimed in any of claims 10 to 21, optionally with some or all of the water therein removed.